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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,451	10/12/2001	Jonathan Braun	P-PM 4968	1617

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EXAMINER	
NAVARRO, ALBERT MARK	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,451	BRAUN ET AL.	
	Examiner	Art Unit	
	Mark Navarro	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-30 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/28/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group VI, claims 31-33 in the response filed October 22, 2003 is acknowledged. The traversal is on the ground(s) that although the claims of Group VI are patentably distinct from those of Group IV, a thorough search of Group VI claims will identify art relevant to Group IV. This is not found persuasive because the separate classification of the groups is one indication of the burdensome nature of the search involved. As set forth in the restriction mailed August 22, 2003, Group IV, is classified in 424, 184.1, while the instantly elected invention is classified in 435, 7.1. This clearly indicates that separate searches within the US Patents must be undertaken. Furthermore, the literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. Applicant's arguments are not found to be persuasive in view that a search of the prior art may reveal a reference which anticipates the method of diagnosing, but does not necessarily anticipate or render obvious the method of treating or preventing Crohn's disease. For these reasons the restriction requirement is deemed to be proper and is adhered to.

Consequently, claims 1-36 are pending in the instant invention, of which claims 1-30 and 34-36 are withdrawn from further consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

2. Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of diagnosing Crohn's disease comprising detecting SEQ ID NO: 2 or 3, does not reasonably provide enablement for methods of diagnosing Crohn's disease comprising detecting pbra or immunoreactive fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir 1999).

Salgaller et al (Cancer Immunol Immunother. Vol. 39, pp 105-116, 1994) teach that in patients with melanoma, cytolysis of target cells pulsed with the synthetic MAGE-1 decapeptide KEADOTGHSY was superior to that of cells pulsed with the immunodominant nonapeptide. Single amino-acid or even side chain substitutions in the immunodominant nonamer abrogated

cytolysis. The cytotoxic T lymphocyte (CTL) lysed target cells expressing the MAGE-1 nonapeptide, including established tumor cell lines, and immortalized EBV-B lines pulsed with peptide. Yet it did not lyse targets pulsed with a peptide containing amino acid substitutions of the natural nonamer. Thus single amino-acid deletions or substitutions have been shown to reduce recognition by CTL. This reference demonstrates that even a single amino acid substitution, deletion or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein.

Fox (U.S. Patent Number 4,879,213) sets forth that "without knowing a protein's three dimensional structure there is no reliable method for determining which linear segments of the protein are accessible to the host's immune system" and that "whether the three dimensional structure is known or not, short linear polypeptides often appear not to have the ability to mimic the required secondary and tertiary conformational structures to constitute appropriate immunogenic and antigenic determinants." (See column 3)

Concerning the Wands analysis, Applicant's specification provides no guidance or working examples as to which "immunoreactive fragments" of pbra are useful for diagnosing Crohn's disease, nor of pbra molecules with the exception of those specifically identified by SEQ ID NO: 2 or 3. (Factors II and III). Furthermore, as shown in the art by Fox and Salgaller et al, altered proteins, and protein fragments are frequently not capable of binding the same molecules as the full length unmodified protein. Consequently one of skill in the art would be forced into excessive experimentation to identify which "substantially the same as pbra" molecules are capable of diagnosing Crohn's disease and furthermore which "immunoreactive fragments" of pbra are able to mimic the required secondary and tertiary structure of the full

length polypeptide, and which fragments are capable of complexing with the antibody that recognizes the full length polypeptide.

3. Claims 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of "pbra" and "immunoreactive fragments."

Applicants define the term "pbra" on page 24, which sets forth that "pbra means a polypeptide having substantially the same amino acid sequence as the *P. fluorescens* pbra polypeptide SEQ ID NO: 2 or the *P. fluorescens* pbra polypeptide SEQ ID NO: 3."

However, one of skill in the art would be unable to determine the metes and bounds of the term "substantially the same." For instance, at what level of identity are the proteins substantially the same? (e.g. 90%, 80%, 40%, 10 %, etc.). Without a clear definition as to the metes and bounds of the term "substantially the same" one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

Likewise, claim 33 recites the sequence of the pbra molecule being claimed, (SEQ ID NO: 2 or 3), however applying the same standards of "substantially the same" to the immunoreactive fragments, one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Targan et al.

The claims are drawn to a method of diagnosing Crohn's disease in a individual, comprising obtaining a sample from said individual, contacting said sample with pbra, or an immunoreactive fragment thereof, under conditions suitable to form a complex of prba, or said immunoreactive fragment thereof, and antibody to pbra, and detecting the presence or absence of said complex, wherein the presence of said complex indicates that said individual has Crohn's disease.

Targan et al (US Patent Number 5,932,429) disclose of methods of diagnosing Crohn's disease comprising determining the presence of ANCA, pANCA, SAPPA, and anti-*Saccharomyces cerevisiae* antibodies in a sample. (See abstract and Examples).

Given that Targan et al have disclosed of methods of diagnosing Crohn's disease in an individual comprising obtaining a sample from an individual and detecting a complex to indicate that the individual has Crohn's disease, the disclosure of Targan et al is deemed to anticipate the claimed invention.

It is noted that Targan et al do not disclose of the molecule "pbra." However, given Applicant's definition of "substantially the same as pbra" the molecule disclosed by Targan is deemed to be substantially the same as pbra, given that both molecules share the same function of being able to diagnose Crohn's disease. Furthermore, the molecule disclosed by Targan et al is also deemed to comprise an immunoreactive fragment of pbra (SEQ ID NO: 2 or 3) for the very same reason.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (703) 306-3225.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Mark Navarro
Primary Examiner
January 6, 2004